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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/578,361	05/24/00	MAES T	4409US

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EXAMINER	
STRZELECKA,T	
ART UNIT	**PAPER NUMBER**
1656	6

DATE MAILED: 12/06/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/578,361	MAES ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-4, 7, 9-11, 18, 19 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koes et al. (PNAS USA, Vol. 92, pp. 8149-8153, 1995), Souer et al. (The Plant Journal, Vol. 7, pp. 677-685, 1995) and Shalon et al. (Genome Research, Vol. 6, pp. 639-645, 1996).

A) Koes et al. describe a method of preparing an insertion element mutant library of transposable elements dTph1 in petunia plants. They describe pooling plant material from three sets of 1,000 plants each in patterns of blocks, rows and columns, e.g. 10 blocks, 10 rows, 12 columns (page 8150, col. 2, par. 4,5; Fig. 2, 3). The mutations are identified using primers complementary to the insertion element and gene to be knocked out (page 8149, col. 2, par. 4).

B) Souer et al. teach a method of isolating gene insertion mutants in petunia plants based on the amplification of insertion element dTph1 flanking sequences using a combination of iPCR and differential screening of amplification products (page 678, col. 1, par. 1). Amplification by iPCR comprises:

i) digesting genomic DNA using a restriction enzyme,

ii) self-ligation of the digested fragments to form circles, and

iii) amplification with an insertion element specific primer (page 678, col. 2, last paragraph; Fig. 2).

Amplification yield can be improved by using re-amplification with nested primers complementary to the insertion element (page 680, col. 1, par. 1). When the insertion element sequences are unknown, several restriction enzymes can be used for the digest (page 680, col. 2, par. 1). The amplified sequences thus produced can be labeled and used as probes to detect the mutated gene(s) (page 682, col. 2, par. 1; page 684, col. 2, par. 2, 3).

C) Shalon et al. teach a method of analyzing complex DNA samples by using microscopic arrays of DNA fragments attached to glass substrate. Such arrays can be used for hybridization screening of genomic DNA. Hybridization probes can be labeled with fluorescent dyes, for example fluorescein (Abstract, page 643-644).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have used the gene insertion mutant library produced by the method of Koes et al. in the screening method of Souer et al. with a reasonable expectation of success. The motivation to do so would have been that gene insertion mutant library was produced rapidly and re-used in different screens, requiring only a limited set of primers, and the amplified fragments were used as probes for screening cDNA or wild-type genomic libraries. In addition, hybridization screening was made more efficient by using microarrays of a large number of DNA fragments attached to a solid support.

3. Claims 5, 6, 8 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koes et al., Souer et al. and Shalon et al. as applied to claim 1 above, and further in view of Vos et al. (Nucleic Acids Res., Vol. 23, pp. 4407-4414, 1995).

A) Claims 5 and 6 are drawn to "transposon display amplification" comprising:

i) digesting nucleic acid sequences from the gene insertion mutant library with two restriction enzymes, one cutting a 6 base pair (bp) site and the other a 4 bp site,

ii) ligating a biotinylated adaptor to the hexacutter site and a second adaptor to the tetracutter site,

iii) selecting biotinylated restriction fragments using streptavidin beads,

iv) amplifying insertion element flanking sequences using primer based on the biotinylated adaptor and insertion element sequence and a primer complementary to the second adaptor,

v) re-amplifying insertion element flanking sequences using nested primer based on the insertion element and a primer complementary to the second adaptor.

Claim 8 is drawn to nucleic acid sequences selected from the group consisting of genomic DNA and cDNA, and claim 12 to using a restriction enzyme from the group consisting of MseI and MunI.

B) Koes et al., Souer et al. and Shalon et al. do not teach amplification by transposon display amplification.

C) Vos et al. teach a DNA fingerprinting technique comprising:

i) digesting DNA with two restriction enzymes, recognizing a 6 bp and 4 bp sites, e.g. EcorI and MseI,

ii) ligating a radiolabelled adaptor to the hexacutter site and a second adaptor to the MseI site,

iii) amplification of the restriction fragments using primers complementary to the adaptors and restriction site sequences.

The fragments could be subjected to a second round of amplification using modified primers (Abstract; page 1408). The amplified fragments can be selected by using a biotinylated adapter for the hexacutter site and separated from the rest of the fragments with streptavidin beads (page 4413, col. 2, par. 3).

It would have been obvious to one of ordinary skill in the art at the time of the invention to have used the DNA amplification method of Vos et al. with the library of gene insertion mutants of Koes et al. eith a reasonable expectation of success. The motivation to do so would have been that amplification and isolation of DNA fragments was achieved without the prior knowledge of their sequences.

4. Claims 13-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koes et al., Souer et al. and Shalon et al. as applied to claim 1 above.

A) Claims 13-17 are drawn to a kit for performing the method of claim 1, comprising DNA samples of an insertion element mutant library, a set of amplified insertion element flanking sequences, which may be fixed to a solid support, be in soluble or dried state or be labeled with fuorescein.

The reagent kits for performing DNA detection assays were conventional in the field of molecular biology at the time of the invention. Therefore it would have been obvious to one of ordinary skill in the art at the time to have packaged the insertion element mutant library and amplified insertion element flanking sequences into a kit for the expected benefits of convenience and cost-effectiveness for practitioners in the art wishing to perform screening for insertion mutants.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at (703) 308-1152. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ts
November 29, 2000
TS

KENNETH R. HORLICK
PRIMARY EXAMINER
GROUP 1600 11/29/00
Kenneth R. Horlick, Ph.D.